REMARKS

The Official Action dated April 20, 2005 has been carefully considered. Accordingly, the present application is now believed to be in condition for allowance. Reconsideration is respectfully requested.

By the present Amendment, claim 28 is amended to clarify that the polymeric form consists of 2-10 monomeric units, and claim 36 is amended to recite the previously designated component "b)". It is believed that these changes do not involve any introduction of new matter, and do not raise any new issues requiring further search and/or consideration, whereby entry is believed to be in order and is respectfully requested.

The Examiner's indication that claims 32-35 are allowed is acknowledged and appreciated.

Claims 28, 30 and 31 were rejected under 35 U.S.C. §103(a) as being unpatentable over the Ferreira et al publication "Dissection of Immunoglobulin E and T Lymphocyte Reactivity of Isoforms of the Major Birch Pollen Allergen Bet v 1: Potential Use of Hypoallergenic Isoforms for Immunotherapy" in view of the Patterson et al U.S. Patent No. 4,269,764 and the Eisenbach-Schwartz et al U.S. Patent No. 6,126,939. The Examiner asserted that it would have been obvious to polymerize the allergen taught by Ferreira et al, in view of Patterson et al, and to use peptide linkers, in view of Eisenbach-Schwartz et al. The Examiner noted that previous claim 29 was not previously rejected because it was drawn to fragments of Bet v 1, while claim 36 encompasses full length allergens of Bet v 1. Further, in response to Applicants' previous arguments, the Examiner asserted that Patterson et al provide a general teaching that any allergen can have its allergenicity reduced by polymerization, referring to column 1, lines 43-50, and that while claims 28 and 36 recite that

the polymeric form (c) has 2-10 monomers, the Examiner interprets the claim as not limited to 10 because the term "having" is open-ended.

However, Applicants submit that the immunogens defined by claims 28, 30, 31 and 36 are nonobvious over and patentably distinguishable from the cited combination of Ferreira et al, Patterson et al and Eisenbach-Schwartz et al. Accordingly, this rejection is traversed and reconsideration is respectfully requested.

Initially, Applicants note that claim 36 is directed to the embodiment comprising a polymeric form of a non-anaphylactic immunogenic recombinant fragment of the protein allergen, the fragment comprising an IgG epitope and an IgE epitope of the protein allergen partly but not completely overlapping, in which form the fragment constitutes the monomeric units. The monomeric units are separated from each other by an oligopeptide linker and the polymeric form of the fragment is recombinantly produced. Thus, claim 36, like previous claim 29, is directed to a polymeric form of the fragment, and not to full length allergens of Bet v 1. Thus, Applicants submit that claim 36, like previous claim 29, is nonobvious over and patentably distinguishable from the combination of cited references. Reconsideration is respectfully requested.

Further, as defined by claim 28, the immunogen according to the present invention is derived from Bet v 1 protein allergen and comprises (a) a non-anaphylactic immunogenic recombinant fragment of the protein allergen, the fragment comprising an IgG epitope and an IgE epitope of the protein allergen partly but not completely overlapping; (b) a polymeric form of the fragment, in which form the fragment constitutes the monomeric units, wherein the monomeric units are separated from each other by an oligopeptide linker; or (c) a non-anaphylactic recombinant polymeric form of the protein allergen consisting of 2 to 10

monomeric units in which the protein allergen constitutes the monomeric units, wherein the monomeric units are separated from each other by an oligopeptide linker. While Applicants' dispute the Examiner's previous contention that "having" is an open-ended term within the context of previous claim 28, current claim 28 is clearly directed to a polymeric form (c) consisting of 2 to 10 monomers. As indicated above, claim 36 is directed to the embodiment (b) of claim 28, recombinantly produced.

Ferreira et al describe their study of T cell activation potency and IgE binding properties of nine isoforms of Bet v 1, namely Bet v 1a-Bet v 1l. Ferreira et al propose allergy treatment with high doses of hypoallergenic isoforms or recombinant variants of atopic allergens, on the assumption that such would modulate the quality of the T helper cell response to allergens in vivo and the therapy form would additionally implicate a reduced risk of anaphylactic side effects.

However, Applicants find no teaching or suggestion by Ferreira et al relating to any of the immunogenic forms defined by (a), (b) or (c) of claim 28, or by claim 36. Moreover, while the Examiner asserts that polymerization, presumably to provide components (b) or (c), or the embodiment of claim 36, would have been obvious in view of Patterson et al and Eisenbach-Schwartz et al, Applicants submit that such a combination is apparent only in view of the teachings of the present specification.

In this regard, Applicants note that Patterson et al disclose ragweed allergens polymerized with glutaraldehyde to produce water-soluble polymers of molecular weights from 200,000 to 20 million. Applicants find no teaching or suggestion by Patterson et al relating to birch pollen allergens, relating to the use of a non-anaphylactic recombinant fragment, or relating to a polymeric form having 2 to 10 monomeric units. In fact, Applicants

find no teaching by Patterson et al relating to the number of monomeric units in their polymers. Thus, the immunogens (a), (b) and (c), and of claim 36, would not have been suggested to one of ordinary skill in the art familiar with Ferreira et al in view of the teachings of Patterson et al relating to ragweed antigens.

While the Examiner asserted that Patterson et al provide a general teaching that any allergen can have its allergenicity reduced by polymerization, referring to column 1, lines 43-50, Applicants find no such teaching by Patterson et al. That is, at column 1, lines 43-50, Patterson et al reference U.S. Patent No. 3,794,630 as disclosing a method for reacting protein allergic extracts with dialdehydes. Patterson et al note that the examples of U.S. Patent No. 3,794,630 disclosed the preparation of such water-insoluble polymerized products from extracts of Cocksfoot pollen and Timothy pollen, but provided no example or reference to ragweed pollen. Thus, not only do Patterson et al not disclose that any allergen can have its allergenicity reduced by polymerization, nor does the referenced U.S. Patent No. 3,794,630 provide such a disclosure, Patterson et al indicate to one of ordinary skill in the art that the teachings of U.S. Patent No. 3,794,630 are limited to the extracts exemplified therein and are not relevant to the ragweed pollen employed by Patterson et al.

On the other hand, Eisenbach-Schwartz et al are directed to dipeptides and pharmaceutical compositions containing a dipeptide for the modulation of immune responses, i.e., a humoral and/or cellular immune response, including, but not limited to, an immune response accompanying inflammation associated with or caused by disease (column 1, lines 37-44). While Eisenbach-Schwartz et al briefly indicate that the peptides, peptide derivatives and compositions may also be useful to treat or ameliorate inflammation associated with, among other things, allergic reactions (column 5, line 22 and column 11, line 25), Applicants

find no teaching or suggestion by Eisenbach-Schwartz et al relating to birch pollen antigens. In fact, the allergic reaction exemplified by Eisenbach-Schwartz et al, namely allergic encephalitis, used as an animal model for multiple sclerosis, is significantly distinguishable from the Bet v 1 protein allergen from which the immunogen defined by claim 28 is derived. Applicants find no teaching or suggestion by Eisenbach-Schwartz et al which would lead one of ordinary skill in the art to combine any of the Eisenbach-Schwartz et al teachings with either Patterson et al or Ferreira et al, particularly in order to form an immunogen as defined by claim 28 or claim 36.

In making a rejection under 35 U.S.C. §103, the Examiner cannot pick and choose among the individual elements of assorted prior art references to recreate the claimed invention; rather the Examiner has the burden to show some teaching or suggestion in the references to support their use in the particular claimed combination, *Smith-Kline Diagnostics, Inc. v. Helena Laboratories Corp.*, 8 U.S.P.Q. 2d 1468, 1475 (Fed. Cir. 1988). Neither the teachings of Patterson et al, specific to ragweed antigens, nor the dipeptide teachings of Eisenbach-Schwartz et al provide any teaching or suggestion for modifying the teachings of Ferreira et al to arrive at the immunogen defined by claim 28 or claim 36. Accordingly, the combination of Ferreira et al, Patterson et al and Eisenbach-Schwartz et al does not render the immunogen defined by claim 28 or claim 36 obvious to one of ordinary skill in the art. It is therefore submitted that claim 28, and claims 30 and 31 dependent thereon, and claim 36 are nonobvious over and patentably distinguishable from the cited combination of Ferreira et al, Patterson et al and Eisenbach-Schwartz et al, whereby the rejection under 35 U.S.C. §103 has been overcome. Reconsideration is respectfully requested.

It is believed that the above represents a complete response to the rejection under 35 U.S.C. §103, and places the present application in condition for allowance. Reconsideration and an early allowance are respectfully requested.

Respectfully submitted,

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